

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Article 36 and Rule 70)

REC'D 28 FEB 2005


WIPO

PCT

Applicant's or agent's file reference 30725	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/SI 03/00036	International filing date (day/month/year) 16.10.2003	Priority date (day/month/year) 18.10.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/20		
Applicant KRKA, TOVARNA ZDRAVIL, D.D., NOVO MESTO et al.		

- This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
- This REPORT consists of a total of 5 sheets, including this cover sheet.  
  
☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  
  
 These annexes consist of a total of 3 sheets.

- This report contains indications relating to the following items:
  - I ☒ Basis of the opinion
  - II ☐ Priority
  - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV ☐ Lack of unity of invention
  - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI ☐ Certain documents cited
  - VII ☐ Certain defects in the international application
  - VIII ☐ Certain observations on the international application

Date of submission of the demand  16.04.2004	Date of completion of this report  25.02.2005
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer  Borst, M  Telephone No. +49 89 2399-8648



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/SI 03/00036

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

**Description, Pages**

1-10 as originally filed

**Claims, Numbers**

1-16 received on 14.02.2005 with letter of 11.02.2005

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/SI 03/00036

---

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes: Claims	1-16
	No: Claims	
Inventive step (IS)	Yes: Claims	1-16
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-16
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/SI 03/00036

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**Documents considered to be relevant to novelty and inventive step**

D1: EP-A-0 830 858 (LILLY CO ELI) 25 March 1998 (1998-03-25)

**1. Novelty (Article 33(2) PCT)**

The subject-matter of independent claims 1 and 16 appears to be new in the light of the prior art available.

D1 (page 5, line 1-51; example 3) discloses tablets obtainable by direct compression from olanzapine particles coated with HPMC, lactose, HPC, microcrystalline cellulose, Croscopovidone and Mg stearate. In contrast thereto the tablets according to the claims on file are obtainable from olanzapine without coating.

**2. Inventive step (Article 33(3) PCT)**

The subject-matter of present claims 1 and 16 appears to involve an inventive step in the light of the prior art available.

The closest prior art D1 (page 2, line 6-21) tries to overcome the metastable properties of olanzapine by coating the olanzapine substance with a polymer. As shown by the experimental data on file (example 2 and 3) for the tablets according to the present claims the stabilisation is achieved in the absence of any olanzapine coating by direct compression of the components (a) to (c).

The objective technical problem to be solved in the light of D1 was, therefore, to provide an alternative, more economic solution to the problem of stabilising olanzapine, in particular against discolouration.

None of the prior art documents available points to the direct compression of olanzapine as defined in claims 1 and 16 for solving the above problem.

**Certain published documents (E) (Rule 64.3 PCT)**

E1: WO 03/086361 A (DESHMUKH ABHIJIT MUKUND ; DHANORKAR VIPIN TATYASAHEB (IN); DIVI MURALI) 23 October 2003 (2003-10-23)

The above-mentioned document does not constitute prior art for the purposes of Article 33(2) and (3) PCT (Rule 64.3 PCT). However, when the present application

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/SI 03/00036

has entered the regional phase at the EPO, said document will be taken into consideration for the examination of novelty.

E1 (example 7-9) discloses tablets comprising olanzapine, about 5% mannitol or sorbit, and about 80% cellulose and pregelatinized starch.

The tablet of E1 (example 13) produced by direct compression comprise olanzapine, cellulose, guar gum and croscopolone. As cellulose and guar gum are polysaccharides the latter formulation not containing a mono- or oligosaccharide is not pertinent to novelty of the claims on file.